REMARKS

Status of the Claims

With this amendment, claims 1-3, 8, 9, 13-27, 30, 31, 33 and 43 have been amended. Support for the amendments can be found throughout the specification and claims as originally filed. Claims 10-12, 42, 45, 49 and 56-58 have been cancelled without prejudice or disclaimer. No new matter has been added.

Claims 1-3, 8-9, 13-27, 30-31, 33, and 41 are pending in the application.

Applicants request reconsideration of the application. Rejections of cancelled claims are considered to be mooted and are not further discussed herein.

Interview Summary

Applicants thank Examiners Rahmani and Seaman for the courtesy of a brief telephonic interview with the undersigned representative on March 19, 2008. During the Interview, the rejections of record were discussed. No final agreement was reached.

Rejections of claims under 35 USC §112, first and second paragraphs

Claims 1-3, 8-9, 13-27, 30-31, 33, and 41 stand rejected under 35 USC §112, first and second paragraphs, as allegedly being indefinite and/or lacking written description. This rejection is traversed.

Without agreeing with the rejections, claims 1-3, 8-9, 13-27, 30-31, 33, and 41 have been amended and no longer recite the language "hydrates thereof". Applicants further contend that claims 1-3, 8-9, 13-27, 30-31, 33, and 41 are clear, are not indefinite, and find written description in the application as originally filed.

Reconsideration and withdrawal of the rejections is proper and the same is requested.

Rejections of claims under 35 USC §112, first paragraph

Claims 33 and 41 stand rejected under 35 USC §112, first paragraph, as allegedly lacking enablement. The Examiner contends that, while Applicants have

shown examples of assays, the "application has not guidance or examples for treating any diseases using the compounds in claim 1." This rejection is traversed.

First, as Applicants have previously contended, the application as filed discloses compounds that have capsaicin modulatory activity, including many working examples, methods of making the compounds, and methods of administering the compounds to a patient for the treatment of the recited conditions. The specification further provides *in vitro* and animal model assays for confirming the compounds' capsaicin modulatory activity and assessing the analgesic efficacy of the compounds in animals. Applicants' disclosure is entitled to consideration for all that it teaches. The Office Action, however, summarily dismisses the *in vitro* and animal model experimental procedures provided in Examples 4 – 10 of the instant application without explanation and does not take into account the extensive discussion of how to make and use compounds and pharmaceutical compositions of the invention, for example, the section spanning page 38, line 25 to page 50, line 4, of the application as filed. Applicants submit that the disclosure of how-to-use, together with the data and routine procedures provided in the specification, are sufficient to allow the selection of appropriate compounds and the determination of treatment protocols for the recited conditions, with only routine experimentation. Accordingly, Applicants respectfully request that the Examiner reconsider the amount of direction or guidance provided in the specification, and Applicants' enablement of the practice of the currently rejected pending method claims.

Second, it is respectfully submitted that the state of the art is such that, in view of the teachings of the present specification, only routine experimentation would be required to practice the claimed invention. *In vitro* and animal models of certain conditions are described in the instant application (see, e.g., Examples 4-10). Moreover, animal models for the therapeutic indications recited in the claims were well known at the time of the present invention, as discussed in a previous response filed by Applicants.

Applicants also wish to point out that efficacy in relevant animal models has, in fact, been confirmed for VR1 antagonists. Applicants have previously supplied examples of patent and literature references describing animal models for certain

claimed therapeutic indications; in some cases, the references also discuss potential treatments of such conditions using VR1 antagonists. Copies of relevant references were supplied with a prior Office Action response.

As a further example, certain VR1 antagonists are presently being tested in human clinical trials as treatments for pain. See, e.g., http://clinicaltrials.gov/ct2/show/NCT00387140?cond=%22Toothache%22&rank=15 (accessed October 17, 2007) (clinical trial of a VR1 antagonist for post-operative dental pain).

Thus, one of ordinary skill in the art could readily use only routine experimentation to confirm the efficacy of compounds in relevant animal models and administer pharmaceutical compositions to a patient in need thereof.

Third, it should be noted that claims 42, 45, 49, and 56-58 have been cancelled without prejudice or disclaimer. Claim 33 is directed to a method for reducing calcium conductance of a cellular capsaicin receptor; claim 41 is directed to a method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*. Applicants respectfully contend that the *in vitro* data presented in the present specification provides ample enablement for the *in vitro* method claims now pending (see claims 33 and 41).

In view of the scope of the claims, the amount of direction and guidance provided by the entirety of Applicants' disclosure, the sophistication of the contemporary state of the art and the high level of skill therein, Applicants believe that it is clear that only routine experimentation would be required to confirm activity of a compound in the relevant animal model, to optimize treatment parameters, and to otherwise practice the full scope of the methods of the pending claims.

Obviousness-Type Double Patenting Rejections

Claims 1-3, 8-27, 30-31, 33, 41, 42, 45, 49, and 56-59 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting (ODP) over certain claims of U.S. Patent Publication 2007-0105865; U.S. Patent Publication 2004-0156869; U.S. Patent Publication 2005-0215575; and U.S. Patent No. 7,074,799. These rejections are traversed.

First, as previously discussed by Applicants in a Response filed October 18, 2007, and as briefly discussed during the Interview, although the Office Action states (at page 10 of the Office Action dated July 18 2007) that the compounds, compositions, and methods of the claims of U.S. Patent Publication 2005-215575 are "fully embraced by" (emphasis in original) and "overlaps mostly significantly" with the present claims, this is not the proper inquiry. To maintain a rejection for obviousness-type double patenting, the Office must establish that the present claims would have been obvious over the claims of the reference patent or patent application. See MPEP 804. The inquiry does not involve the claims of a patent application publication; the focus is on whether the claims of the underlying patent application render obvious the claims of the present application. Thus, the proper inquiry is whether the pending claims of U.S. patent application no. 10/892,741 (the patent application which published as U.S. Patent Publication 2005-215575), now U.S. Patent No. 7,329,664, render obvious the claims of the present application. Applicants contend that they do not.

The instant pending claims are directed to compounds (including salts, and compositions and methods of use thereof) in which the compound includes at least one phosphate or phosphonate group. In contrast, the final claims of the '741 application (now U.S. Patent No. 7,329,664) are directed to specific compounds (and salts thereof); none of the compounds recited in the claims of the '664 patent includes at least one phosphate or phosphonate group, as required by the claims of the instant application. The claims of the '664 patent contain absolutely no teaching or suggestion of this feature of the presently-pending claims. The claims of the '664 patent therefore cannot, and do not, render obvious the claims of the instant application, and the double patenting rejection must be withdrawn.

Second, in the Office Action, certain claims stand rejected (or provisionally rejected) under the judicially-created doctrine of obviousness-type double patenting over certain claims of U.S. Patent No. 7,074,799. However, Applicants note that the instant pending claims are directed to compounds (including salts, and compositions and methods of use thereof) in which the compound includes at least one phosphate or phosphonate group. In contrast, the claims of the '799 patent are directed to compounds (and salts, and pharmaceutical compositions, and methods of use thereof) which differ from the presently-claimed compounds; none of the compounds recited in

the claims of the '799 patent includes at least one phosphate or phosphonate group, as required by the claims of the instant application. The claims of the '799 patent contain absolutely no teaching or suggestion of this feature of the presently-pending claims. The claims of the '799 patent therefore cannot, and do not, render obvious the claims of the instant application, and the double patenting rejection must be withdrawn.

Third, in the Office Action, certain claims stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over certain claims of U.S. Patent Publication No. 2004-0156869 (the publication of USSN 10/735,607 ("the '607 application")). However, Applicants note that the instant pending claims are directed to compounds (including salts, and compositions and methods of use thereof) in which the compound includes at least one phosphate or phosphonate group. In contrast, the pending claims of the '607 application are directed to compounds (and salts, and pharmaceutical compositions, and methods of use thereof) which differ from the presently-claimed compounds; none of the compounds recited in the pending claims of the '607 application includes at least one phosphate or phosphonate group, as required by the claims of the instant application. The pending claims of '607 application contain absolutely no teaching or suggestion of this feature of the presently-pending claims. The claims of the '607 application therefore cannot, and do not, render obvious the claims of the instant application, and the double patenting rejection must be withdrawn.

Fourth, in the Office Action, certain claims stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over certain claims of U.S. Patent Publication No. 2007-0105865 (the publication of USSN 10/571,203 ("the '203 application")). However, Applicants note that the instant pending claims are directed to compounds (including salts, and compositions and methods of use thereof) in which the compound includes at least one phosphate or phosphonate group. In contrast, the pending claims of the '203 application are directed to compounds (and salts, and pharmaceutical compositions, and methods of use thereof) which differ from the presently-claimed compounds; none of the compounds recited in the pending claims of the '203 application includes at least one phosphate or phosphonate group, as required by the claims of the instant application. The pending claims of '203 application contain absolutely no teaching or suggestion of this feature of the presently-pending

claims. The claims of the '203 application therefore cannot, and do not, render obvious the claims of the instant application, and the double patenting rejection must be withdrawn.

Conclusion

Early and favorable consideration of the application is earnestly solicited.

Applicants conditionally petition for an extension of time in the event that an extension is required. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 60425 (72021).

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Respectfully submitted,

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